Tablet Production Example:

| | |
|---|---|
| a) 1) Active ingredient | 30 g |
| 2) Lactose | 95 g |
| 3) Corn starch | 30 g |
| 4) Carboxymethyl cellulose | 44 g |
| 5) Magnesium stearate | 1 g |
| | 200 g for 1000 tablets |

**[0040]** The ingredients 1 to 3 are uniformly blended with water and granulated after drying under reduced pressure. The ingredient 4 and 5 are mixed well with the granules and compressed by a tabletting machine to prepare 1000 tablets each containing 30 mg of active ingredient.

| | |
|---|---|
| b) 1) Active ingredient | 30 g |
| 2) Calcium phosphate | 90 g |
| 3) Lactose | 40 g |
| 4) Corn starch | 35 g |
| 5) Polyvinyl pyrrolidone | 3.5 g |
| 6) Magnesium stearate | 1.5 g |
| | 200 g for 1000 tablets |

**[0041]** The ingredients 1-4 are uniformly moistened with an aqueous solution of 5 and granulated after drying under reduced pressure. Ingredient 6 is added and granules are compressed by a tabletting machine to prepare 1000 tablets containing 30 mg of ingredient 1.

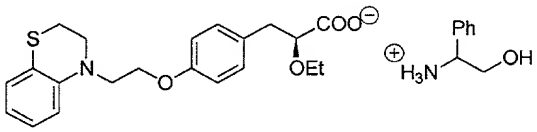
**[0042]** The compound of the formula (I) as defined above are clinically administered to mammals, including man, via either oral, nasal, pulmonary, transdermal or parenteral, rectal, depot, subcutaneous, intravenous, intraurethral, intramuscular, intranasal, ophthalmic solution or an ointment. Administration by the oral route is preferred, being more convenient and avoiding the possible pain and irritation of injection. However, in circumstances where the patient cannot swallow the medication, or absorption following oral administration is impaired, as by disease or other abnormality, it is essential that the drug be administered parenterally. By either route, the dosage is in the range of about 0.01 to about 100 mg/kg body weight of the subject per

day or preferably about 0.01 to about 30 mg/kg body weight per day administered singly or as a divided dose. However, the optimum dosage for the individual subject being treated will be determined by the person responsible for treatment, generally smaller doses being administered initially and thereafter increments made to determine the most suitable dosage.

**[0043]** The invention is explained in detail in the examples given below which are provided by way of illustration only and therefore should not be construed to limit the scope of the invention.

**Example 1**

**S-Phenyl glycinol salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid**




**[0044]** (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (20.89g) and isopropanol (210 ml) were added to 500 ml four necked round bottom flask, fitted with a mechanical stirrer and reflux condenser. The reaction mixture was heated slowly to 45-55°C for complete dissolution of the glassy sticky mass. S-(+) phenyl glycinol (7.4 g) dissolved in isopropanol (75 ml) was added to the reaction mixture at 45-55°C in about 30 min. under stirring. The reaction mixture was maintained for reflux at 80-90°C for 12-14 h and monitored the progress of the reaction. The reaction mixture was brought to temperature of 45-50°C under stirring and maintained for 2-3 hours at 45-55°C. The precipitated product was filtered, dried at 60°C for 2-3 h to afford the pure S-phenyl glycinol salt of (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid as off-white to light cream color crystalline solid (weighs about 22 g, yield : 80%, m.p.: 126-128°C, purity 98-99% by HPLC).

**[0045]** IR (KBr) $cm^{-1}$ : 3450-3300 (O-H stretch), 3060 (-C-H aromatic stretch), 2700 - 2200 ($^{+}NH_3$ band), 2922 (-C-H aliphatic stretch), 1570 ($-COO^-$ stretch), 1400 ($-COO^-$ stretch).

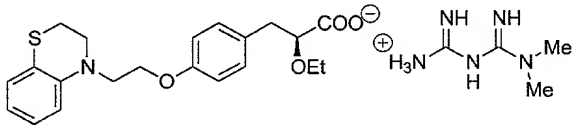
**[0046]** $^1$H NMR (200 MHz, DMSO)δ : 1.0 (t, 3H, $CH_3$-$CH_2$-O); 2.6-3.40 (m, 5H, -S-$CH_2$, Ar-$CH_2$; CH-Ar), 3.45-4.0 (m, 8H, -$CH_2$-N-$CH_2$; $CH_2$-$CH_2$-O, $CH_2$-OH), 4.05 (q, 2H, -$OCH_2$), 4.3 (m, 1H, -CH-OEt), 6.5 (t, 1H, -$CH_2$-OH), 6.7-7.5 (m, 13H, Aromatic).

**[0047]** Mass m/z : 388 ($M^+$ + 1), 138 ($C_8H_{11}O$), 121 ($C_8H_{10}$).

**[0048]** Anal. Calcd for $C_{29}H_{36}N_2O_5S$, %C 66.41; % H 6.87; %N 5.34; Found %C 66.35, %H 6.74, %N 5.25.

## Example 2

## Metformin salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid




**[0049]** (-)-3-[4-[2-(3,4-Dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid (3.87 g) and isopropanol (40 ml) were added to 250 ml four necked round bottom flask, fitted with a mechanical stirrer and reflux condenser. The reaction mixture was slowly heated to 45-55°C for complete dissolution of the glassy sticky mass. Metformin (1.29 g) dissolved in isopropanol (20 ml) was added to the reaction mixture at 55-65°C in about 10 min. under stirring. The reaction mixture was maintained for reflux at 75-85°C for 12-14 hours and monitored the progress of the reaction. The reaction mixture was cooled to room temperature and stirred for 2-3 h at room temperature. The precipitated product was filtered, dried at 60°C for 2-3 h to afford the pure metformin salt of (-)-3-[4-[2-(3,4-dihydro-2H-1,4-benzothiazin-4-yl)ethoxy]phenyl]-2-ethoxy propanoic acid as cream color crystalline solid (weighs about 3.1 g, yield : 78 %, m.p.: 155-158°C, purity: 99 % by HPLC).

**[0050]** IR (KBr) $cm^{-1}$ : 3430-3300 (N-H stretch), 3053 (-C-H aromatic stretch), 2700 - 2200 (-$NH_3$ band), 2922 (-C-H aliphatic stretch), 1660 (-COO stretch), 1400 (-COO stretch).

**[0051]** $^1$H NMR (200 MHz, $CD_3OD$)δ : 1.0 (t, 3H, $CH_3$-$CH_2$-O), 2.6-3.40 (m, 11H, -S- $CH_2$, Ar-$CH_2$, CHAr, -$NMe_2$), 3.45-3.80 (m, 6H, -$CH_2$-N-$CH_2$, -$CH_2$-$CH_2$-O-), 4.2 (t, 2H, -$CH_2$-$CH_2$-O), 6.5 (t, 1H, -$CH_2$-CH-), 6.65-7.2 (m, 8H, aromatic).